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Public Health Reports

Treasury Department, United States Marine-Hospital Service. Published in accordance with act of Congress approved February 15, 1893.

VOL. XII.

WASHINGTON, D. C., JULY 30, 1897.

No. 31.

UNITED STATES.

[Reports to the Supervising Surgeon-General United States Marine-Hospital Service.]

The yellow fever bacillus of Sanarelli and Havelburg.

No. 123a POTSDAMER STRASSE,
Berlin, Germany, July 11, 1897.

SIR: I have the honor to transmit herewith, for your consideration, Annales de l'Institut Pasteur, Vol. XI, No. 6, June 25, 1897, which has particular interest at this time as containing the article of Dr. Sanarelli, of Montevideo, on yellow fever, and a résumé of the article of Dr. Havelburg, of Rio de Janeiro, on the same subject. With the publication of these articles they become the common property of the scientific world, and it is the privilege of anyone to criticise or lend adherence to their doctrines as may to him seem justified by experience and observation. Therefore, I would simply invite your attention to the fact that there is in this particular publication presented the strange coincidence of two earnest workers, laboring independently and at some distance from each other upon the same disease, and in each case claiming in no uncertain terms to have discovered the specific organism of a malady which always has had, and probably will so long as time lasts ever have, a vast interest for the people and the Public-Health Service of the United States. Not only have the claims been made, but each claimant has submitted with his brief a specimen, presumably authentic, of his so-called specific microbe.

A very brief and cursory examination of the two papers will show that Drs. Havelburg and Sanarelli have worked with and have described two totally different microbes—organisms which I can testify, from personal observation, can not by any possibility be confounded or reconciled with each other. I think that therefore it may be considered as having almost the value of an axiom, that if one is right the other is certainly wrong, and it remains for us to judge for ourselves which of the

two bacilli in question shall enjoy the claim of being the cause beyond peradventure of the disease which, above all others perhaps, has for more than a hundred years occupied the thought and time of some of the brightest minds of two continents, and which was a subject of controversy long before the bacterial origin of disease was admitted, and during a period when the germ origin of disease was a theory, and a theory capable of no scientific demonstration.

It is now several years ago that Koch formulated the essentials which must be filled by a microorganism before it could be considered as the specific cause of any given disease, and they are so succinct, so simple, and yet so crucial, that they have not been called into question to this day. In part, they are (a) that the organism must always be found in the blood, organs, or tissues of men and animals sick with or recently dead of a given disease; (b) that isolated and in pure culture it must be capable, when introduced into the economy of men and animals, of reproducing the disease. For our purposes these are the essentials of his four postulates.

Do the organisms under consideration fill these simple and yet crucial conditions? Let us take first the organism vaunted by Dr. Havelburg. He claims that by injecting, subcutaneously or intraperitoneally, some of the stomach contents of a patient suffering with, or dead from, yellow fever, into a guinea pig that the animal will inevitably succumb, and that consequently it has succumbed to yellow fever. Admitting, for the sake of argument, that this is invariably true, does it necessarily follow that a so called yellow fever germ has produced that disease, and that death is due to this cause alone? I think not. In experiments of this kind we must not lose sight of the fact that in the normal intestinal canal there are organisms which, while apparently purely saprophytic, can, under certain conditions not as yet fully understood, become highly pathogenic. Chief among these organisms must be mentioned a bacillus, or rather a group of bacilli, formerly considered purely saprophytic, but to which of late a high degree of pathogenic power has been attributed. I refer to the "*bacterium coli commune*" or to the group of organisms of which this is the type. Under certain conditions this apparently normal and inoffensive denizen of the intestinal canal may become highly pathogenic, and induce either suppuration or more generally intoxications by the production and liberation of toxins.

The characteristics of the colon bacillus are, in brief, a rod-shaped bacillus, with a tendency to assume filamentous forms, or in young cultures a species of elongated oval coccus; growing well in all ordinary culture media; coagulating milk; producing fermentation in bouillon containing lactose, with an evolution of carbon dioxide; rendering alkaline culture media acid, as evidenced by the change in color of litmus; the production of indol; lastly the production, in animals submitted to experimental inoculation, of peritonitis, pleurisy, pericarditis, hepatitis, with a special tendency to the retention of the biliary secretions, renal engorgements, and finally uræmia.

Compare these characteristics with the claims of the organism of Havelburg, and when to all of these are added an appearance of growth upon gelatine, agar-agar, potato, and in bouillon very characteristic of the colon bacillus, I think it must be admitted that Havelburg has simply added another one to the list of investigators who have fallen victims to the deceptive appearances of this omnipresent colon bacillus.

Again, is it true that the inoculation of the stomach contents of a yellow fever patient into a guinea pig will always cause illness or death

to the animal? The experiments of Sternberg and others would show that the inoculation and ingestion of large or small quantities of yellow fever stomach and intestinal contents into dogs, rabbits, guinea pigs, and other domestic animals, while sometimes followed by death, is usually attended by purely negative results.

Taking all these facts into consideration, therefore, I have no hesitation in reporting to you that the case of Dr. Havelburg is, to say the least, not proved, and that so far as he is concerned, *the specific microbe of yellow fever is not yet discovered*. The consideration of the organism of Dr. Sanarelli presents more difficulties, and can not be dismissed from our report as coming under the head of an error in interpretation of results. Here we have an organism with which we are up to this time unfamiliar; an organism certainly pathogenic, and in the majority of cases producing death when injected subcutaneously or intraperitoneally into guinea pigs. Consideration of the article of Dr. Sanarelli will show that he has formulated a theory of the infection of yellow fever which is at once new and in some respects startling to those familiar with the disease. Certainly it admits of no argument that the chief pathological changes in yellow fever are found in the stomach and upper portion of the small intestine, the liver and the kidneys; that death comes in one of three ways, either by a profound intoxication early in the malady, by the exhaustion to which the hemorrhages certainly contribute, or lastly by uræmia, due to the suppression of the urinary secretion, owing to the degenerative changes which exist in the kidneys. Therefore it is startling to be informed that the infection of the disease probably enters through the respiratory tract, that the organism is elaborated in the blood, that the well-known pathological changes are due to toxine poisoning, and that death is, in many cases, owing to a secondary infection from the colon and other bacilli normally resident in the stomach and intestinal canal. This is hard to believe, nor is it easier to accept the theory that yellow fever is a cyclical disease when we are told in his preliminary remarks on symptomatology that death may occur on from the second to the eighth day. Certainly the cycle is not well marked, for not only is there thus a very wide variation in the time of death, but when the virulence of the organism is increased by special methods of culture the time of death of the animal inoculated is vastly hastened, and again the question occurs, where is the cyclical characteristic?

Further, Dr. Sanarelli informs us that he has not found his bacillus in every one of the very small number of cases which he has examined, in fact it was wanting in very nearly 50 per cent of these cases, and while for this failure he gives us a sufficiently specious reason, still he has failed to fulfill the first postulate, viz, that the organism must be constantly found in the blood, organs, or tissues of men or animals sick with or recently dead of the disease. Has he succeeded any better in the second one, that the organism injected in pure culture into susceptible animals must invariably produce the disease in question? Unfortunately, it may be objected that the action of a given organism upon a guinea pig is not a sure index of its action upon the human economy. Nevertheless it is the best resource at our disposition and I am compelled to say, that after witnessing several necropsies of animals killed by the bacillus of Sanarelli, that I could find nothing in the microscopical appearances of the organs, especially of the liver, which was suggestive to me of yellow fever. I can only suggest that it will require extensive investigation of a very large number of cases of the disease,

the much more constant finding of the bacillus in question, and its trial on animals more closely allied to man, before the claims set forth can be accepted. Dr. Sanarelli promises further contributions on the subject. Indeed, I am informed that the manuscript of a second memoir had been received by the editors of the *Annales de l'Institut Pasteur* just prior to my departure from that institution. Possibly, therefore, it will be fairer to suspend judgment until his complete work on the subject has appeared, but it has been suggested that a fair plan would be to investigate the formation of toxines by the organism of Sanarelli, to endeavor with these toxines to immunize an animal, and then to ascertain if there is a corresponding production of antitoxines, to be evidenced by protection afforded to animals, both against the toxines and the culture itself. This would seem to me to be the most feasible plan, and I hope, in the interest of science, that it will be faithfully carried out.

Through the kindness of Professor Roux I am in possession of cultures of the organisms of both Havelburg and Sanarelli, and for much of the information herein contained I am indebted to Professor Novy, of Ann Arbor, Mich., who was investigating the questions at the Institut Pasteur.

Very respectfully, yours,

H. D. GEDDINGS,
Passed Assistant Surgeon, U. S. M. H. S.

Yellow fever reported in Martinique and Puerto Rico.

DELAWARE BREAKWATER QUARANTINE STATION,
via Lewes, Del., July 23, 1897.

SIR: I have the honor to inform you that the master of the American schooner *Lelia Smith* states that yellow fever is prevailing on the Island of Martinique, and that yellow fever and smallpox exist in Puerto Rico. The *Lelia Smith* is just from St. Johns, Antigua, having previously come from New York to Guadeloupe. The master states that Guadeloupe has quarantined against Martinique, and while he was at Guadeloupe a vessel (French) arrived from Martinique, and was put in quarantine; that it was reported that 1 man died from yellow fever while the vessel was in quarantine, on or about June 20, 1897. He states that Antigua and Gaudeloupe are clean, and no contagious diseases are there. He brings clean bills of health. The public health reports of July 16 make no mention of any yellow fever, either at Martinique or Puerto Rico, and recent arrivals at this station from St. Pierre, Martinique, have all brought clean bills of health, viz: Italian bark *St. Anna*, arrived July 12, seventeen days on voyage, and Italian bark *Maria*, arrived July 15, thirteen days on voyage. The statements of the master of the *Lelia Smith* were corroborated by the steward. In view of the absence of any other information to the contrary, it might be well to investigate these statements.

Respectfully, yours,

C. P. WERTENBAKER,
Passed Assistant Surgeon, U. S. M. H. S.

Plague on the British ship Annie Maud.

NATIONAL QUARANTINE STATION,
Angel Island, Cal., July 16, 1897.

SIR: I have the honor to report the British ship *Annie Maud*, one hundred and forty-three days from Calcutta, was placed in quarantine to-day for disinfection. A short while after leaving Calcutta one of the